PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex Parte Ding et al.

Appeal No. _____

In re Application of:	**DING et al.**
Serial Number:	09/268,437
Filed:	March 12, 1999
Art Unit:	1641
Examiner:	Gailene R. Gabel
Appellants:	Ying Ding, Brian Halsall and William R. Heineman
Title:	**SIMULTANEOUS MULTIANALYTE ELECTROCHEMICAL ASSAY BASED ON SPATIAL RESOLUTION**
Attorney Docket:	UOC-134A

Cincinnati, Ohio 45202 September 27, 2005

Mail Stop Appeal Brief-Patents
Commissioner for Patents and Trademarks
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPEAL BRIEF

I. Real Party in Interest

The real party in interest is The University of Cincinnati, Cincinnati, Ohio.

II. Related Appeals and Interferences

There are no related pending appeals or interferences. Applicant filed a Notice of Appeal and Brief in April, 2003. However, the Examiner chose to issue a new grounds of rejection and prosecution was reopened.

III. Status of Claims

Claims 1-9, 11 and 12 are pending in the application. Claims 6-9 are subject to a restriction requirement, and have been withdrawn from consideration.

Claims 1-5, 11, and 12 are rejected, and are the subject of this Appeal.

IV. Status of Amendments

No amendments have been filed subsequent to the final rejection dated March 28, 2005.

V. Summary of Claimed Subject Matter

The claimed invention is a simultaneous electrochemical assay device comprising a cell adapted to hold a sample and a plurality of working electrodes adapted to quantitatively measure enzymatic reaction product.

The goal of the invention is to detect multiple analytes in a single sample using different analyte binding areas situated at distinct, separate locations, and a plurality of working electrodes located within proximity of those distinct, separate locations (page 3, lines 6-10). The assay detects labeled enzymatic reaction product that are either electroactive or catalyze the production of an electroactive product (page 2, lines 5-6).

The invention requires location of each working electrode adjacent to one analyte binding area, with each working electrode measuring the presence of a certain analyte and being separated from the nearest adjacent analyte binding area by a predetermined distance (page 5, lines 1-9). Enzymatic reaction product is actually measured. Any analyte bound to any analyte binding area will product this same enzymatic reaction product. Since the working electrode for each binding area is spatially separated from adjacent binding areas, a measurement can be taken before cross-

interference is created by diffusion of reaction product from an adjacent analyte binding area (page 12, lines 13-16; page 13, lines 3-7).

The predetermined distance between adjacent analyte binding areas is estimated by using the Einstein equation (page 5, lines 9-17). This distance is the minimum distance necessary to prevent cross-interference between the electrode measuring one type of analyte and the electrode at a second analyte binding site (page 12, lines 5-16). The calculation of this predetermined distance is based upon the physical phenomenon of Fickian diffusion (page 5, lines 1-17; page 12, lines 5-16).

Further, the electrodes are placed in close proximity to their respective analyte binding areas in order to detect actual enzyme reaction product, i.e. the electrodes do more than merely detect electrochemiluminescence (ECL) created by a reporter agent (see page 5, lines 1-9, and page 3, lines 10-15). Indeed, quantitative measurement of enzyme reaction product by the working electrodes is one reason why an individual working electrode must be separated from an adjacent analyte binding area by a predetermined distance. That is, the reaction product from the enzyme at a first analyte binding site will not diffuse in sufficient quantity to interfere with the working electrode at an adjacent analyte binding site (see page 5, lines 4-9). Therefore, the predetermined distance between analyte binding areas is a distance which is effective to permit each electrode to measure the analyte bound to its adjacent analyte binding site, yet prevent that electrode from inadvertently measuring an interfering amount of analyte bound to the nearest adjacent analyte binding site.

The assay device of this invention is applicable to any electrochemical technique which utilizes an electrode, including chronoamperometry, cyclic voltammetry, linear scan voltammetry, pulse voltammetry, and differential pulse voltammetry (see page 9, lines 1-11). The diameter of the electrodes, the width of the antibody immobilization strips, and the distances between

detection electrodes are preferably on the "millimeter" scale. However, the scale can be extended to the "micrometer" scale for the above stated dimensions, and is also extendable down to the "nanometer" scale using recently developed methodologies for depositing conducting materials with dimensions in this regime (see page 16, lines 3-17).

VI. Grounds of Rejection to be Reviewed on Appeal

A. Claims 1-5, 11 and 12 were rejected under 35 U.S.C. §112.

B. Claims 1-5, 11 and 12 are rejected under 35 U.S.C. §102(e) as anticipated by Henkens et al. U.S. Patent 6,391,558.

C. Claims 11-12 are rejected under 35 U.S.C. §102(b) as anticipated by Cozzette et al. U.S. Patent 5,063,081.

VII. Argument

A. Claims 1-5, 11 and 12 are not indefinite under 25 U.S.C. § 112 second paragraph.

The Examiner has indicated that because claim 1, and claims dependent thereon, includes the recitation "adapted to receive a sample", it is unclear, and was rejected under 35 U.S.C. § 112, second paragraph. It is applicant's contention that one skilled in the art, upon reading the specification, would clearly understand the meaning of "adapted to receive a sample", and, therefore, the claim is not objectionable under 35 U.S.C. § 112, second paragraph.

In reviewing a claim for compliance with 35 U.S.C. § 112 second paragraph, one must consider the claim as a whole to determine whether the claim appraises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. § 112 second paragraph. See *Soloman v. Kimberly Clark*, 55 USPQ 2nd 1279, 1283 (Fed. Circ. 2000).

Claim 1 claims a simultaneous electrochemical assay device. To recite that the device is adapted to receive a sample, is almost redundant. But, certainly this phrase does not create ambiguity as to the meaning of the claim. If one considers the specification, the figures show the drawing of the cell as well as the location of the sample on the cell. Although the disclosure is diagrammatic, it simply shows a planar surface upon which a sample can be received or located. Further, one skilled in the art would know the meaning of "a cell adapted to receive a sample" for an electrochemical assay device.

The Examiner's position with respect to claim 1 is that "adapted to receive a sample" is unclear because it does not specify how the cell is modified to perform its intended function. "For example, 1) does the cell have a channel connected thereto adapted to receive a sample. See also claim 11."

Whether the cell had a channel adapted to receive a sample, or is simply a planar surface where surface tension holds the sample, is irrelevant with respect to clarity. The claim need not be limited to provide clarity. There is certainly nothing (either in the form of an argument or evidence) presented by the Examiner that would suggest that one skilled in the art would fail to understand the scope of the claims because of the use of the terminology. For that reason, it is applicants' position that the claims are not indefinite under 35 U.S.C. § 112 second paragraph.

B. Claims 1-5, 11 and 12 are not anticipated in light of the reference of Henkens et al. U.S. Patent 6,391,558 under 35 U.S.C. § 102(e)

1. Henkens is not an appropriate reference under 35 U.S.C. § 102(e)

Applicants present application has an effective filing date of March 16, 1998, which was the filing date of the original provisional application. The Henkens reference was filed as a provisional

application on March 18, 1997. A continuation-in-part application was filed on March 17, 1998, subsequent to applicants' effective filing date. The Examiner is now citing the disclosure of this continuation-in-part application (now patent) as if it has the same disclosure as the provisional application filed March 18, 1997. That is improper. The fact that it is a continuation-in-part indicates that the patent's specification is not the same as the original provisional application. Any regular application based on a provisional application is not necessarily the same as the disclosure of the provisional application. Therefore, the Examiner cannot rely on the disclosure in this patent, and, accordingly, it is an improper reference. As this is the only reference cited against claims 1-5, claims 1-5 should be allowed.

2. The Henkens reference (if an appropriate reference) does not anticipate applicants' present invention

Claim 1 reads:

> 1. A simultaneous electrochemical assay device comprising a cell adapted to receive a sample, said cell having a surface having a plurality of analyte binding areas, each of said analyte binding areas having a different specific analyte binding substrate; and a plurality of working electrodes adapted to quantitatively measure enzymatic reaction product, each working electrode adjacent to one analyte binding area and separated from the nearest adjacent analyte binding area by a distance and a common reference electrode for said plurality of working electrodes wherein said device does not have means to mix a sample in said cell.

Claim 1 recites that there is a common reference electrode for a plurality of working electrodes. The second independent claim, claim 11, reads:

> 11. An electrochemical assay device comprising a cell adapted to receive a sample and simultaneously test multiple different analytes, said cell having a surface having a plurality of analyte binding areas, each of said analyte binding areas having a different specific analyte

> binding substrate; and a plurality of working electrodes and each working electrode adjacent to one analyte binding area and separated from the nearest adjacent analyte binding area by a distance, all of said binding areas coated with a single quiescent solution containing substrate reactive with enzymes bonded to analyte binding areas wherein said device does not have means to mix a sample in said cell.

Claim 11 does not require a common reference electrode for a plurality of working electrodes. It claims the apparatus in use with "all of said binding areas coated with a single quiescent solution containing substrate reactive with enzymes bonded to analyte binding areas." Thus, this has one solution with the reactive substrate coating the binding areas.

The Henkens et al. reference discloses an assay apparatus which utilizes a plurality of working and reference electrodes in a biosensor array. These are, for example, screen printed onto a circuit board with a plurality of labeled nucleic acid segments attached to the surface of the working electrodes. The labeled segments generate an electric current when electric potential is applied to the working electrode after the attached labeled nucleic acid segments are hybridized or annealed with a target nucleic acid. This specifically requires a one-to-one relationship of working and reference electrodes.

The Henkens et al. reference discloses and requires separate reference electrodes for each working electrode. This reference does not disclose a structure designed to test multiple analytes simultaneously.

Thus, whereas applicants' invention is relying on the rate of diffusion of product through the sample area, the Henkens et al. reference requires a plurality of electrodes to be utilized to generate a plurality of different signals. The Henkens et al. reference is not disclosing the same apparatus as claimed in applicants invention. The Examiner has totally ignored the limitation in claim 1 that there

is a common reference electrode for the plurality of working electrodes. This limitation is also present in claim 12, dependent upon independent claim 11.

Claim 11 claims the apparatus actually in use wherein the multiple binding areas are coated with a single quiescent solution containing substrate reactive with enzymes bonded to analyte binding areas. That is not disclosed in the Henkens et al. reference. They do not use or disclose multiple binding areas coated with a single quiescent solution containing "substrate reactive with enzymes bonded to the analyte." In light of that, it cannot be considered in anticipation of claim 11.

Further, the Henkens et al. reference actually discloses a separate well for each different electrode. As disclosed in Column 20, lines 53-56, the three electrodes are contained within a bean-shaped depression which serves as a sample well. Thus, these are clearly not used in a way wherein a common solution of substrate reactive with the enzymes would be coated onto multiple analyte binding areas. Thus, the Henkens et al. reference also fails to disclose the limitation in new claim 11.

Further, applicants' would point out that it is not obvious to modify Henkens et al. to arrive at applicants' invention, although it is not cited under 35 U.S.C. § 103. It is not designed to rely on the same solution migration characteristics of the analyte in order to effectively measure multiple different materials. It fails to disclose this. It, rather, uses separate pairs of working and reference electrodes to provide the ability to measure different nucleic acids.

C. Claims 11 and 12 are not anticipated by the disclosure of Cozzette et al. U.S. Patent 5,063,081

The Cozzette et al. reference, as the title would suggest, discloses a method of manufacturing a plurality of uniform microfabricated sensing devices having an immobilized ligand receptor. It discloses formation of multiple assay devices on a single silicon chip, and subsequently cutting these

in to individual chips. Primarily, the disclosure is intended to describe making a plurality of the same electrochemical devices. Each working electrode requires a separate reference electrode. There are some limited references to forming different assay devices on the same chip, but these do not use analyte binding areas as claimed by applicants' invention. For example, the primary discussion of multiple assay devices is at column 58, lines 38-47. These would be detecting sodium, potassium or chorine in addition to ammonia. None of these would rely on analyte binding areas. There is also disclosure of a combined electrode which analyses glucose and cholesterol. But these use glucose oxydase and cholesterol oxydase, and do not have specific analyte binding areas, as claimed in the pending application.

Claim 11 specifically claims that applicants' device has the multiple binding areas which are coated with a single quiescent solution containing substrate reactive with enzymes bonded to analyte binding areas. Thus, the sample is positioned on the cell and the different analytes would bond to the binding area. A solution containing substrates reactive to enzymes bonded to analyte binding areas would then be placed on the cell. Any analyte which was bonded, whether the same or different, would then produce an electrical signal. By quickly monitoring the signal from the respective electrodes positioned adjacent the binding areas, one can determine specifically which proteins are present. That is not disclosed in the Cozzette et al. reference. They do not use a single quiescent solution containing substrate reactive with enzymes bonded to the analyte binding area. For that reason, it cannot be used in the same manner as applicants' invention.

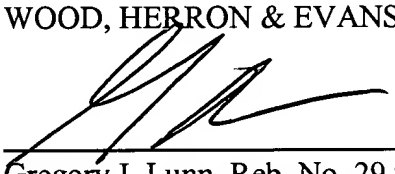
Further, with respect to claim 12, this requires that there be a common reference electrode for a plurality of working electrodes. The Cozzette et al. reference requires a one-to-one relationship of reference electrodes to working electrodes. Thus, it cannot anticipate claim 12 for this reason.

D. Conclusion

In light of the above, it is applicants' position that the claims are not indefinite under 35 U.S.C. § 112. Those skilled in the art would clearly understand what "adapted to receive a sample" means. Further, the Henkens et al. reference was not an appropriate reference under 25 U.S.C. § 102(e). Further, even if it were, it does not anticipate any of the claims of the pending application. Finally, claims 11 and 12 were not anticipated by the disclosure of the Cozzette et al. reference. In light of this, applicants would respectfully request that the Examiner's rejection of the pending claims be reversed.

Respectfully submitted,

WOOD, HERRON & EVANS, L.L.P.



Gregory J. Lunn, Reb. No. 29,945

2700 Carew Tower
441 Vine Street
Cincinnati, OH 45202
(513) 241-2324 (voice)
(513) 241-6234 (facsimile)

Claim Appendix

Claims Involved in the Appeal

1. (Previously presented) A simultaneous electrochemical assay device comprising a cell adapted to receive a sample, said cell having a surface having a plurality of analyte binding areas, each of said analyte binding areas having a different specific analyte binding substrate; and a plurality of working electrodes adapted to quantitatively measure enzymatic reaction product, each working electrode adjacent to one analyte binding area and separated from the nearest adjacent analyte binding area by a distance and a common reference electrode for said plurality of working electrodes wherein said device does not have means to mix a sample in said cell.

2. (Previously presented) The device claimed in claim 1 wherein said binding substrates each comprise a plurality of different analyte specific proteins.

3. (Previously presented) The device claimed in claim 1 wherein said binding substrates each comprise a different antigen.

4. (Previously presented) The device claimed in claim 1 wherein said binding substrate comprises a different antibody.

5. (Previously presented) The device claimed in claim 1 further comprising at least one auxiliary electrode in said cell.

6. (Withdrawn) A method of testing for a plurality of different analytes in a test solution using a test cell having a plurality of spaced analyte binding sites wherein each binding site is specific for a separate analyte;

locating separate electrodes adjacent to each binding site and spaced from an adjacent binding site;

adding a test solution to said cell;

adding reagent to said cell wherein portions of said reagent react with each of said analytes and wherein said reagent includes at least one label

electrochemically detecting said label at each of said electrodes in less than a time in which label-produced product at any binding site can migrate to an adjacent binding site.

7. (Withdrawn) The method claimed in claim 6 wherein said label contains an enzyme and further comprising adding substrate to said cell wherein said label is detected by measuring a reaction product of said enzyme and said substrate.

8. (Withdrawn) The method claimed in claim 7 wherein said product is measured amperometrically.

9. (Withdrawn) The method claimed in claim 6 wherein said binding site comprises a plurality of analyte specific proteins and said reagent comprises a plurality of analyte specific proteins each labeled with the same label.

10. (Canceled)

11. (Previously presented) An electrochemical assay device comprising a cell adapted to receive a sample and simultaneously test multiple different analytes, said cell having a surface having a plurality of analyte binding areas, each of said analyte binding areas having a different specific analyte binding substrate; and a plurality of working electrodes and each working electrode adjacent to one analyte binding area and separated from the nearest adjacent analyte binding area by a distance, all of said binding areas coated with a single quiescent solution containing substrate reactive with enzymes bonded to analyte binding areas wherein said device does not have means to mix a sample in said cell.

12. (Previously presented) The assay device claimed in claim 11 wherein said device has a common reference electrode for said plurality of working electrodes.

Evidence Appendix

No evidence has been submitted pursuant to Sections 1.130, 1.131, or 1.132.

Related Proceedings

There are no decisions rendered by a Court or Board in any proceeding identified pursuant to Paragraph C(1)(ii).

INDEX